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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,880	12/13/2001	Nurith Kum	492692000300	9067
25226	7590	01/12/2004	EXAMINER	
MORRISON & FOERSTER LLP 755 PAGE MILL RD PALO ALTO, CA 94304-1018			SPIEGLER, ALEXANDER H	
			ART UNIT	PAPER NUMBER
			1637	
DATE MAILED: 01/12/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/017,880

Applicant(s)

KURN, NURITH

Examiner

Alexander H. Spiegler

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 January 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-185 is/are pending in the application.
- 4a) Of the above claim(s) 16-31, 56-81, 97-112, 137-162, 166-167 and 172-185 is/are withdrawn from

consideration.

- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15, 32-55, 82-96, 113-136, 163-165 and 168-171 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                               | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2/20/02</u> . | 6) <input type="checkbox"/> Other: _____                                    |

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PTO-326 (Rev. 04-01)

**Offic Action Summary**

**Part of Paper No. 2004**

## **DETAILED ACTION**

### ***Status of the Application***

1. This action is in response to Applicants' response, filed on August 14, 2003. Currently, claims 1-3, 6-34, 36-84, 87-115, 117-185 are pending, Claims 16-31, 56-81, 97-112, 137-162, 166, 167 and 172-185 have been withdrawn, and Claims 1-3, 6-15, 32-34, 36-55, 82-84, 87-96, 113-115, 117-136, 163-165 and 168-171 are currently under consideration and are rejected. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn. Specifically, 112, 2<sup>nd</sup> paragraph rejections have been withdrawn in view of Applicants' amendments and arguments.

### ***Information Disclosure Statement***

2. The information disclosure statement of February 20, 2002 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

### ***Double Patenting***

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-15, 32-55, 82-96, 113-136, 163-165, 168-171 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-116 of U.S. Patent No. 6,251,639 in view of Soderlund et al. (USPN 6,013,431).

Claim 1 of the instant application recites:

1. A method of generating multiple copies of a nucleic acid sequence of interest, said method comprising the steps of:

(a) hybridizing a composite primer to a target polynucleotide, wherein the composite primer comprises an RNA portion and a 3' DNA portion, the 3' DNA portion comprising a 3' most nucleotide, such that 3' most of the 3' DNA portion hybridizes from about 1 to about 10 nucleotides from the sequence of interest.;

(b) extending the composite primer with DNA polymerase under conditions that permit primer extension, whereby a primer extension product is produced; and ;

(c) cleaving the RNA portion of the primer extension product of (b) with an enzyme that cleaves RNA from an RNA/DNA hybrid such that the cleaved primer extension product dissociates from the target polynucleotide,

wherein the primer extension product is of a size that when the RNA is cleaved the cleaved primer extension product dissociates from the target polynucleotide under essentially the same conditions as those for primer extension, whereby multiple copies of the sequence of interest are produced.

Similarly, claims 1-2 of '639 recite:

1. A method for amplifying a polynucleotide sequence complementary to a target polynucleotide sequence comprising:

(a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion;

(b) optionally hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template;

(c) extending the composite primer with DNA polymerase;

(d) cleaving the RNA portion of the annealed composite with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer hybridizes to the template and repeats primer extension by strand displacement,

whereby multiple copies of the complementary sequence of the target sequence are produced.

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2. A method for amplifying a target polynucleotide sequence comprising:

(a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion;

(b) optionally hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template;

(c) extending the composite primer with DNA polymerase;

(d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer hybridizes to the template and repeats primer extension by strand displacement to produce displaced primer extension product;

(e) hybridizing a polynucleotide comprising a promoter and a region which hybridizes to the displaced primer extension product under conditions which allow transcription to occur by RNA polymerase, such that RNA transcripts are produced comprising sequences complementary to the displaced primer extension products,

whereby multiple copies of the target sequence are produced.

Additionally, claim 23 is drawn to "characterizing a sequence of interest in a target polynucleotide, and claim 27 is drawn to "detecting a mutation in a target polynucleotide" using the amplification reaction in either claim 1 or 2.

Therefore, the claims of '639 differ from the claims of the instant application in that does not disclose the limitation that the 3' most nucleotide of the 3' DNA portion of the primer hybridizes from about 1 to about 10 nucleotides from the sequence of interest.

However, hybridizing a primer near a sequence of interest is well known in the art to aid in identifying variations. For example, Soderlund et al. teaches the hybridization of the 3' most nucleotide of the 3' DNA portion of a primer for identifying single nucleotide variations (see Figs. 1-3, cols. 3-9). Soderlund also teaches many of the common methodologies accompanying amplification and detection reactions, such as the use of probes; solid supports, and labels (cols. 3-17).

In view of the teachings of Soderlund et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of '639

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so as to have included the steps of hybridizing 3' most nucleotide of the 3' DNA portion of the primer from about 1 to about 10 nucleotides from the sequence of interest, in order to have achieved the benefit of providing an effective means of detecting and identifying nucleotide variations.

### **Applicants Arguments**

Applicants argue the instant invention does not recite the limitation of "another composite primer hybridizes to the template and repeats primer extension by strand displacement", which occurs in Claim 1(d) of the '639 patent. Applicants argue the Examiner did not show a suggestion or motivation to modify the teaching of the '639 patent to delete or modify step 1(d) of the '639 patent. Applicants also argue Claim 2 of the '639 patent does not teach the same limitations of the instant invention, and that the claims of the '639 patent teach additional limitations not required by the instant claims.

### **Response to Applicants Arguments**

Applicants' arguments have been considered, but are not persuasive for several reasons. First, all of the pending claims are drawn to methods "comprising", which therefore allows for additional limitations to be present in the claims of the '639 patent that do not appear in the instant invention. Accordingly, because the instant claims are drawn to methods "comprising" (which allows for additional limitations other than the limitations specified) there does not need to be a motivation or suggestion to remove the additional limitations that may occur in the '639 patent and do not occur in the instant claims.

Applicants' argument with respect the differences between Claim 1 of the '639 patent and the instant claims is also not persuasive. Applicants' argue Claim 1(d) of the '639 patent and

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Claim 1(c) of the instant invention are patentably distinct because Claim 1(d) has an additional limitation that “another composite primer hybridizes to the template and repeats primer extension by strand displacement”. However, Claim 1(d) ‘639 patent necessarily includes the limitations of instant claim 1. That is, before any addition of another composite primer (as taught by the ‘639 patent), the RNA from an RNA/DNA hybrid is cleaved, and the cleaved primer extension product dissociates from the target polynucleotide, wherein the primer extension product is of a size that when the RNA is cleaved the cleaved primer extension product dissociates from the target polynucleotide under essentially the same conditions as those for primer extension, whereby multiple copies of the sequence of interest are produced. Specifically, instant Claim 1(c) occurs before the adding of another composite primer, and thus the addition of the composite primer is an additional step to the instant claims. This can be seen in Figure 1 of the instant invention. In Figure 1, the RNA is cleaved from the RNA/DNA hybrid (by RNase H); the extended cleaved primer extension product is dissociated such that another composite primer hybridizes to the template and repeats primer extension by strand displacement. Thus, the dissociation of the cleaved primer extension product must necessarily precede the addition of another composite primer. Since the instant claims are drawn to methods “comprising”, the additional step of cleaving the hybrid “such that another composite primer hybridizes to the template” is permitted and still reads on the claimed invention.

Accordingly, the rejection is maintained.

### *Conclusion*

5. No claims are allowable.



6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

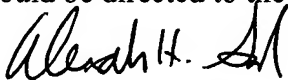
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*Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806 or (571) 272-0788 after January 22, 2004. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (703) 308-2199 or at (571) 272-0747 after January 13, 2004. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119 or at (571) 272-0782 after January 22, 2004. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler  
January 7, 2004



GARY BENZION, PH.D.  
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